

METHODS AND COMPOSITIONS UTILIZING QUINAZOLINONES

CROSS-REFERENCE TO RELATED APPLICATION

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This application claims priority under 35 USC 119(e) from U.S. Provisional Application No. 60/198,253, having Jeffrey T. Finan as the inventor, filed October 27, 1999, and titled "METHODS AND COMPOSITIONS UTILIZING QUINAZOLINONES", which is incorporated by reference herein for all purposes; it also claims priority under 35 USC 119(e) from U.S. Provisional Patent Application No. 60/213,104, having Jeffrey T. Finan et al. as inventors, filed June 21, 2000, and titled "METHODS AND COMPOSITIONS UTILIZING QUINAZOLINONES", which is incorporated by reference herein for all purposes.

FIELD OF THE INVENTION

This invention relates to quinazolinone derivatives which are inhibitors of the mitotic kinesin KSP and are useful in the treatment of cellular proliferative diseases, for example cancer, hyperplasias, restenosis, cardiac hypertrophy, immune disorders and inflammation.

BACKGROUND OF THE INVENTION

Interest in the medicinal chemistry of quinazoline derivatives was stimulated in the early 1950's with the elucidation of the structure of a quinazoline alkaloid, 3-[β -keto-gamma-(3-hydroxy-2-piperidyl)-propyl]-4-quinazolinone, from an Asian plant known for its antimalarial properties. In a quest to find additional antimalarial agents, various substituted quinazolines have been synthesized. Of particular import was the synthesis of the derivative 2-methyl-3-o-tolyl-4-(3H)-quinazolinone. This compound, known by the name methaqualone, though ineffective against protozoa, was found to be a potent hypnotic.

Since the introduction of methaqualone and its discovery as a hypnotic, the pharmacological activity of quinazolinones and related compounds has been investigated. Quinazolinones and derivatives thereof are now known to have a wide